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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/316,955	05/22/99	MELIEF	C 98-4

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HM22/1010

EXAMINER	
BECKERLEG, A	

ART UNIT	PAPER NUMBER
1632	16

DATE MAILED: 10/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/316,935	MELIEF ET AL.	
	Examiner	Art Unit	
	Anne M Beckerleg	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *8-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment and arguments received on 7/31/01 have been entered. This application contains claims 8-13, which have been withdrawn from consideration as being drawn to an invention non-elected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 1-7 are active in the instant application. An action on the merits follows.

Applicant's submission of a paper copy of the sequence listing and CRF which include SEQ ID NO:3 is acknowledged. This application is now in sequence compliance.

Applicant's amendment to the specification indicating that this application claims benefit to U.S. provisional application 60/086,625 is acknowledged.

Those sections of Title 35, US code, not included in this action, can be found in the previous office action, paper no. 8.

The rejection of claim 4 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of applicant's amendment to the claims.

The rejection of claims 1-3, and 5-7 under 35 U.S.C. 112, first paragraph, for lack of written description is withdrawn in view of applicant's arguments and supporting publications from the prior art.

The rejection of claims 1-7 under 35 U.S.C. 112, first paragraph, for scope of enablement is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons or record as discussed in detail below.

As stated in the previous office action, the specification, while being enabling for pharmaceutical compositions comprising a monoclonal antibody directed against CD40 and the HPV16 E7 peptide having the sequence of SEQ ID NO. 3 suspended in IFA, and methods of reducing tumor growth of an E7 expressing tumor by subcutaneously administering the pharmaceutical composition wherein the anti-CD40 antibody is species matched to the recipient, does not reasonably provide enablement for pharmaceutical compositions comprising any CTL activating peptide or the use of said compositions to treat any tumor or infectious disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The specification discloses the treatment of infectious disease or tumors by administering a pharmaceutical composition comprising a CTL activating peptide and a CD40 binding protein

which is an antibody. It is noted that the specification clearly identifies the use of the disclosed pharmaceutical compositions to treat disease, particularly cancer.

The applicant argues that the use of the term "CTL-activating" sufficiently describes the properties of the encompassed peptides such that the skilled artisan would understand which types of peptides meet the claim limitations. The office acknowledges that peptides which bind to MHC class I and stimulate CTL were known at the time of filing. However, as discussed in detail in the previous office action, the specification fails to provide sufficient guidance as to the physical or biological characteristics of peptides other than the E7 peptide having the sequence of SEQ ID NO:3 which are capable of having a therapeutic effect on any disease when administered *in vivo* in combination with an anti-CD40 antibody. As discussed in the previous office action, the two CTL activating peptides described by the specification each comprise a single MHC class I epitope. The potential immune response to vaccination with a single MHC class I epitope is limited to a CTL response as the epitopes described do not bind to MHC class II. While low affinity antibodies might be generated by the peptides, it is unlikely that such antibodies would recognize the parent protein in view of protein folding and conformation. In terms of generating a therapeutic CTL response, the specification does not provide sufficient guidance as to the level of CTL response against a single peptide epitope which correlates with protection against any type of infection or against tumor growth and development. The specification does not specifically identify any infectious diseases which can be treated using the instant methods or identify infections which can be successfully treated by generating a CTL response alone. Further, the

specification does not provide sufficient guidance as to the affects of the route of administration on CTL generation or demonstrate that injection of peptide and anti-CD40 either systemically or locally at any site in the body can generate therapeutic CTL activity.

The applicants argue that since the binding of CD40 results in the activation of dendritic cells which are then capable of priming naive CTL, this mechanism of T cell priming should provide the same response to any infectious disease or tumor. This is not compelling in view of the teachings of Yasutomi et al. that CTL generation alone is not sufficient to treat viral infections such as SIV, and in view of the teachings of Restifo et al. that many types of tumors are capable of evading the immune response by down regulating molecules associated with the MHC class I pathway (Yasutomi et al. (1995) J. Virol., Vol. 69 (4), page 2279; and Restifo et al (1993) J. Immunother., Vol. 14, page 183, col 1, lines 8-14, and page 184, col. 2).

Further, it is noted that the example utilizes a species matched anti-CD40 antibody. It was well known at the time of filing that the administration of xenogeneic proteins, such as antibodies, results in an immune response against the foreign protein. In view of the strong immune response against xeno-antigens, the skilled artisan would not be able to predict whether a xeno-anti-CD40 antibody would persist in sufficient quantity in a patient to have any effect on peptide specific CTL generation. The applicant has not provided any arguments concerning this issue.

Therefore, in the absence of guidance from the specification as to the level of CTL generation against a peptide epitope which is sufficient to treat any neoplastic disease or infection in the absence of a humoral response, the art recognized unpredictability of protecting against

infection based on a CTL response alone, and the difficulties involved in immune recognition of tumors, and the breadth of the claims, the skilled artisan would not have predicted success in treating any tumor or infection by administering any CTL activating peptide in combination with an anti-CD40 antibody.

The rejection of claims 1-7 under 35 U.S.C. 103 for lack of obviousness over Feltkamp in view of Anderson is withdrawn in view of applicant's arguments.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Marie S. Beckerleg, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 10:30-7:00. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The official fax number is (703) 308-4242.

Dr. A.M.S. Beckerleg

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER